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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,930	07/21/2003	Vicki Bowman Vance	9536-3	6465

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Karen A. Magri
Myers Bigel Sibley & Sajovec
Post Office Box 37428
Raleigh, NC 27627

EXAMINER

KUMAR, VINOD

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,930	VANCE ET AL.	
	Examiner	Art Unit	
	Vinod Kumar	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-19, 21, 22, 24 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20, 23 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>08/10/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 20, 23 and 26 are examined. This action is made **FINAL**.
2. The objection to specification is withdrawn light of amendments to the specification.
3. The rejection to claims 20, 23 and 26 under 35 U.S.C. 102(b)/103(a) is withdrawn in view of claim amendments.

Claim Rejections - 35 USC § 112

4. Claims 20, 23 and 26 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a plant cell or plant transformed with miRNA precursor construct comprising a promoter operably linked with miRNA 167 precursor sequence which comprises a sequence that is complementary to a portion of target sequence of interest, does not reasonably provide enablement for a plant cell or plant transformed with any miRNA precursor construct comprising any miRNA sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for the reasons of record stated in Office action mailed May 16, 2006. Applicants traverse the rejection in the paper filed August 10, 2006.

Applicants argue that the presently claimed invention is enabled for a wide variety of miRNA precursors, in addition to the miRNA 167 and miRNA 171 precursors disclosed. In addition, Applicants argue that numerous publications describe what constitutes an miRNA precursor and how these precursors are identified. Applicants further argue that based on the commonly shared features of miRNA precursors and the teachings of the present specification, one skilled in the art would expect that a wide variety of miRNA precursors could be used as a backbone to produce a functional miRNA via the miRNA biogenesis pathway (response, page 11, lines 3-18). Applicants further argue that since the specification teaches how to design and use miRNA precursors of the present application, it enables one of skill in the art to use a multiplicity of miRNA precursors as backbones to produce functional miRNAs via the miRNA biogenesis pathway that can be used to stably transform a plant or plant cell (response, page 13, lines 6-11).

Applicant's arguments were fully considered but were not persuasive. The specification does not provide guidance on a method of designing (making) any miRNA precursor construct. The specification does provide guidance on making miRNA 167 precursor construct which comprises a portion of a sequence that is complementary to a portion of target sequence, such as GUS. Designing a miRNA precursor comprising a sequence which is complementary to the target sequence of interest would require prediction analysis of said precursors to form an irregular hairpin structure containing various mismatches, internal loops and bulges so that the predicted precursor molecule forms most favorable structure in solution. This involves extensive analysis of secondary structures of the predicted miRNA precursors and selecting the structure with

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lowest free energy, so that predicted non-natural miRNA precursor is effectively processed and produces gene silencing effect when expressed in a plant cell or plant. The specification does not provide any guidance how such prediction analysis would be carried out and what parameters would be used in predicting said structures so that artificially designed miRNA precursor molecules would undergo normal biogenesis to release miRNAs when expressed in a plant. Furthermore, it is important to note that the instantly claimed invention encompasses naturally occurring polycistronic miRNA precursors designed to comprise a sequence which is complementary to a portion of a gene sequence of interest. The specification provides no guidance on making said polycistronic miRNA precursors which would undergo normal biogenesis to produce stable miRNA when introduced and expressed in a plant. In the absence of such guidance, it would have been highly unpredictable at the time claimed invention was made that any miRNA precursor design comprising any non-native sequence which is complementary to a portion of target mRNA sequence of interest would be effectively processed to produce a stable miRNA product, and subsequently participate in producing gene silencing effect when expressed in a plant cell or plant. Applicants have failed to provide guidance as to how inoperable embodiments can be readily eliminated other than random trial and error.

To further address Applicant's arguments, Applicant's attention is specifically drawn to page 1623, 2nd paragraph of column 1 through the end of first paragraph of column 2 of Reinhart et al. reference which was cited in the Applicant's response filed on August 10, 2006 (page 11, lines 3-8), wherein it is clearly taught that differences exist in the structure and production of miRNA precursors from diverse sources, such

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as, animals, plants, metazoan etc. The differences include cellular compartmentalization, timing of precursor processing or types of cofactors involved in processing of miRNA. This implies that even naturally occurring miRNA precursors derived from diverse sources may not be able to undergo normal biogenesis to produce a stable miRNA when expressed in plants. The instantly claimed invention encompasses any miRNA from any source and Applicants have provided no guidance on the method of using miRNA precursor derived from diverse sources. Applicants have not provided guidance how one skilled in the art would design instantly claimed miRNA precursor which would undergo normal biogenesis when expressed in the plant cell or plant to participate in regulating the expression of a gene of interest. In the absence of guidance, undue experimentation would have been required by a skilled artisan to determine how to make and use any miRNA precursor comprising a sequence which is complementary to a target sequence of interest.

Accordingly, the rejection is maintained.

5. Claims 20, 23 and 26 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record stated in Office action mailed May 16, 2006. Applicants traverse the rejection in the paper filed August 10, 2006.

Applicants argue that amended claims meet written description requirements because amended claims recite an miRNA precursor construct or miRNA precursor

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rather than RNA precursor construct or precursor RNA, respectively (response, page 13, lines 17-21).

Applicant's arguments were fully considered but were not persuasive. Claims 20, 23 and 26 encompass any miRNA precursor construct comprising any miRNA precursor sequence which comprises any miRNA sequence carrying a sequence that is complementary to a portion of a target sequence of interest. The specification does not have adequate written description for the genus miRNA precursor sequences, and genus of miRNA sequences comprising a sequence complementary to a target sequence of interest under current written description guidelines. Applicants have failed to describe these undisclosed structures of their broadly claimed genus, and one skilled in the art cannot reliably predict these structures based on the disclosure of miRNA 167 precursor. The claims encompass structures of a broadly claimed genus whose function has not been correlated with regulating the expression of a target sequence of interest when expressed in a plant cell or plant. Applicants have failed to describe common functional domains or elements shared by these undisclosed structures. Thus, it is evident that Applicant's broadly claimed genus was not reduced to practice. Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing.

Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 20, 23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Llave et al. (The Plant Cell, 14:1605-1619, Published July 1, 2002, Applicant's IDS) in view of Valvekens et al. (PNAS, 85:5536-5540, 1988). This rejection is necessitated due to claim amendments.

Llave et al. teach a number of plant miRNA precursors including miRNA 5 or miRNA 35 (also known as miRNA 167) comprising miRNA sequences. Reference also teaches that miRNA precursor processes to produce miRNA molecule which are involved in regulating gene expression through post-transcriptional gene silencing. The reference further teaches that miRNA comprise a sequence which is complementary to a portion of an endogenous gene sequence which is regulated by said miRNA. The reference also teaches that actual regulatory role of large number of plant miRNA sequences is not understood. See in particular, page 1605, abstract; page 1608, table 1; page 1609, figure 4; page 1611, table 2; page 1612, table 3; page 1613, figure 6; page 1614, figure 7; page 1617, accession numbers.

Llave et al. do not teach a method of producing a transgenic plant.

Valvekens et al. teach a method of transformation of plant cells and regeneration of transgenic plants expressing heterologous protein. See page 5536, column second through column 1 of page 5537; page 5538, Figures 3 and 4.

It would have been obvious to one of ordinary skill in the art at the time claimed invention was made to use any Llave et al. miRNA precursor including miRNA167 which naturally comprise a sequence having complementarity to a portion of an endogenous

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gene sequence, in a method of producing a transgenic plant using any plant transformation method including the one taught by Valvekens et al. One of the ordinary skill in the art would have been motivated to overexpress any Llave et al. miRNA precursors including miRNA167 in a plant for the purpose of determining their role in plant growth and development with reasonable expectation of success.

Thus, the claimed invention as a whole was prima facie obvious over the combined teachings of the prior art.

Summary

7. Claims 20, 23 and 26 are rejected.

Applicants amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is set to expire within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



ASHWIN D. MEHTA, PH.D.
PRIMARY EXAMINER